

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 September 2005 (15.09.2005)

PCT

(10) International Publication Number
WO 2005/084104 A3

(51) International Patent Classification⁷: **C07D 221/12**, (74) Agents: **WILD, Robert** et al.; c/o ALTANA Pharma AG, A61K 31/473, C07D 401/12 Byk-Gulden-Str. 2, 78467 Konstanz (DE).

(21) International Application Number: PCT/EP2005/051025

(22) International Filing Date: 8 March 2005 (08.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
04100959.8 9 March 2004 (09.03.2004) EP
05100545.2 27 January 2005 (27.01.2005) EP

(71) Applicant (for all designated States except US): **ALTANA PHARMA AG** [DE/DE]; Byk-Gulden-Str. 2, 78467 Konstanz (DE).

(72) Inventors (for all designated States except CA, PH, US): **SCHMIDT, Beate**; Allensbacher Str. 5, 78476 Allensbach (DE). **FLOCKERZI, Dieter**; Ackerweg 26, 78476 Allensbach (DE). **HATZELMANN, Armin**; Alter Wall 3, 78467 Konstanz (DE). **ZITT, Christof**; Mainaustr. 209 D, 78464 Konstanz (DE). **BARSIG, Johannes**; Bleichenweg 11, 78467 Konstanz (DE). **MARX, Degenhard**; Obere Reute 15, 78345 Moos (DE). **KLEY, Hans-Peter**; Im Weinberg 3b, 78476 Allensbach (DE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **KAUTZ, Ulrich** [DE/DE]; Prof.-Schmider-Str. 12, 78476 Allensbach (DE).

(74) Agents: **WILD, Robert** et al.; c/o ALTANA Pharma AG, Byk-Gulden-Str. 2, 78467 Konstanz (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.

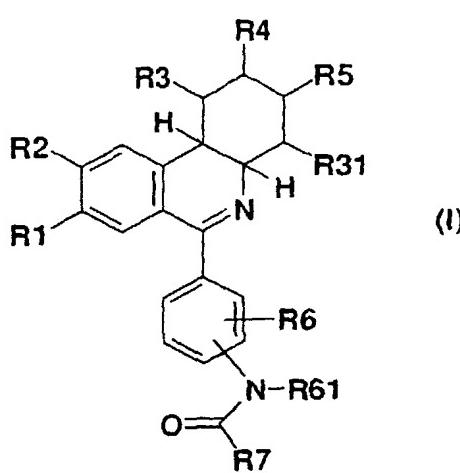
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,

[Continued on next page]

(54) Title: NOVEL ISOAMIDO-SUBSTITUTED HYDROXY-6-PHENYLPHENANTHRIDINES AND THEIR USE AS PDE4 INHIBITORS



(57) Abstract: Compounds of a certain formula (I), in which R1 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy, R2 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy, or in which R1 and R2 together are a 1-2C-alkylenedioxy group, R3 hydrogen or 1-4C-alkyl, R31 is hydrogen or 1-4C-alkyl, either, in a first embodiment (embodiment a) according to the present invention, R4 is -O-R41, in which R41 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-7C-alkylcarbonyl, or completely or predominantly fluorine-substituted 1-4C-alkyl, and R5 is hydrogen or 1-4C-alkyl, or, in a second embodiment (embodiment b) according to the present invention, R4 is hydrogen or 1-4C-alkyl, and R5 is -O-R51, in which R51 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-7C-alkylcarbonyl, or completely or predominantly fluorine-substituted 1-4C-alkyl, R6 is hydrogen, halogen, 1-4C-alkyl or 1-4C-alkoxy, R61 is hydrogen, 1-4C-alkyl or 1-4C-alkoxy-2-4C-alkyl, R7 is Het1, Har1, 3-7C-cycloalkyl, or 1-4C-alkyl substituted by R8, are novel effective PDE4 inhibitors.



NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
— of inventorship (Rule 4.17(iv)) for US only

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
13 October 2005

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.